

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

GLYCOLIC ACID

Chemical Code # 934, Tolerance # 50298

10/1101

I. DATA GAP STATUS

Combined, rat:	No study on file ¹
Chronic toxicity, dog:	No study on file ¹
Oncogenicity, mouse:	No study on file ¹
Reproduction, rat:	No study on file ¹
Teratology, rat:	No data gap; no adverse effect
Teratology, rabbit:	No study on file ¹
Gene mutation:	No data gap; no adverse effect
Chromosome effects:	Not required at this time ²
DNA damage:	No data gap; no adverse effect
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through # 175863 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

indicates a study on file but not yet reviewed.

File name: T183818.doc

Leung, 10/11/01

¹ This new active ingredient was submitted as an antimicrobial and these studies are not required at this time.

² Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals Series 84, Mutagenicity, Addendum 9, EPA- 540/09-91-122, PB91-15158394.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study on file.

CHRONIC TOXICITY, RAT

No study on file.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

** 007; 175853; "Developmental Toxicity Study of Glycolic Acid in Rats"; (S.M. Munley; E.I. duPont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Report No. 191-96; 6/20/96); Twenty five mated Sprague-Dawley female rats/group were treated by oral gavage with 0, 75, 150, 300 or 600 mg/kg/day of Glycolic Acid (purity: 99.6%) from day 7 through day 21 of gestation. No mortality resulted from the treatment. Animals in the highest dose group exhibited signs of irregular respiration, lung noise, lethargy and abnormal gait. The mean body weight gain of the 600 mg/kg group was less than that of the control ($p < 0.05$). The incidences of malformations, developmental variations and variations due to developmental retardation were increased for the 600 mg/kg treatment group. The mean fetal weight for the highest dose group was less than that of the control ($p < 0.05$). **No adverse effect indicated. Maternal NOEL:** 300 mg/kg/day (based upon the lower body weight gain and the clinical signs demonstrated by the 600 mg/kg/day treatment group); **Developmental NOEL:** 300 mg/kg/day (based upon the increased incidence of malformations, developmental variations and variations due to developmental retardation and lower mean fetal weight of the 600 mg/kg/day treatment group); **Study acceptable.** (Moore, 10/5/00)

TERATOLOGY, RABBIT

No study on file.

GENE MUTATION

** 012; 175861; "Glycolic Acid 70% Solution: Bacterial Reverse Mutation Test in *Salmonella typhimurium* and *Escherichia coli*"; (N.L. Gladnick; E.I. du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Project ID: DuPont-1301; 8/27/98); *S. typhimurium* strains TA97a, TA98, TA100 and TA1535 and *E. coli* strain WP2 *uvrA* (pKM101) were incubated for 48 hours at 37° C with Glycolic Acid 70% Solution (a.i.: 70.58%) at concentrations ranging from 1.0 to 5000 µg a.i./plate in two trials under conditions of non-activation and activation. Each treatment level was plated in triplicate. An S9 fraction derived from the liver of young male Sprague-Dawley rats pretreated with Aroclor 1254 was used to metabolize the test material. There was no treatment-related increase in the incidence of reverse mutation. **No adverse effect indicated. Study acceptable.** (Moore, 10/17/00)

** 013; 175862; "Glycolic Acid 70% Solution: L5178Y TK⁺ Mouse Lymphoma Forward Mutation Assay with a Confirmatory Assay"; (M.A. Cifone; Covance Laboratories Inc., Vienna, VA; Project ID: DuPont-1616; 10/15/98); Mouse lymphoma L5178Y cells (clone 3.7.2C (TK⁺)) were treated with Glycolic Acid 70% Solution (a.i.: 70.58%) at concentrations ranging from 39.3 to 5000 µg a.i./ml in the first trial and 250 to 5000 µg a.i./ml (65.8 mM) in the second trial for 4 hours at 37° C under conditions of activation and non-activation. The determination of mutant frequency was performed in triplicate for each treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. A mutagenic response was evident for the activated samples at treatment levels ≥ 2500 µg a.i./ml (mutant frequency > 2x that of the control value). However, the concentration of the test material was in excess of the treatment concentration limit of 10 mM and therefore, not considered to be a positive response. **No adverse effect indicated. Study acceptable.** (Moore, 10/16/00)

CHROMOSOME EFFECTS

No study on file.

DNA DAMAGE

** 014; 175863; "Glycolic Acid 70% Solution: Mouse Bone Marrow Micronucleus Assay"; (L.R. Cox; E.I. duPont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Project ID: DuPont-1197; 10/20/98); Five CD-1 mice/sex/time point (unless otherwise indicated) were dosed orally by gavage with 0, 1200 (males), or 1600 (females) mg/kg of Glycolic Acid 70% Solution and euthanized at 24 and 48 hours after dosing. In addition, 5 mice/dose were dosed with 300 or 600 (males), or 400 or 800 (females) mg/kg of the test material and euthanized at 24 hours after dosing. Five animals/sex were similarly dosed with 40 mg/kg of cyclophosphamide as the positive control and euthanized 24 hours after dosing. In order to assure that 5 animals/sex/dose were available for testing, 5 additional males were dosed with 1200 mg/kg and 3 additional females with 1600 mg/kg of the test material. Five of these males and 3 of the females died over the course of the study. Clinical signs included lethargy, moribundity and abnormal gait. Bone marrow samples from the femur were examined and the percentage of polychromatic erythrocytes (PCE) with a micronucleus and the ratio of PCE to normochromatic erythrocytes were determined. No treatment-related increase in the number of micronucleated PCE's was noted. No adverse effect indicated. Study acceptable. (Moore, 11/6/00)

NEUROTOXICITY

No study on file.

SUBCHRONIC STUDY

50298-011; 175859; "Glycolic Acid 70% Solution: Subchronic Toxicity 90-Day Gavage Study in Rats

with Immunotoxicity, Neurotoxicity, and One-Generation Reproduction Evaluations"; (K.H. Kreckmann; E.I. duPont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Project ID: DuPont-1597; 8/13/99); Forty Crl:CD (SD)IGS BR rats/sex/group were dosed orally by gavage with 0, 150, 300 or 600 mg a.i./kg/day of Glycolic Acid 70% Solution (a.i. 70.58%). Ten animals/sex/group each were designated for the subchronic toxicity, the immunotoxicity, the neurotoxicity and the reproduction toxicity studies. In the subchronic toxicity and neurotoxicity studies, the animals were treated for 13 weeks. The Immunotoxicity assessment was performed by injecting Sheep Red Blood Cells (SRBC) in the tail vein of the assigned animals on day 23 and euthanizing the animals on day 29. In the reproduction study, the animals were dosed for 13 weeks and throughout the mating, gestation and lactation periods. Two males in the 600 mg/kg group (one in the subchronic study and one in the reproduction study) died due to apparent treatment-related causes. One male in the control group, one male and one female in the 300 mg/kg group and one male and four females in the 600 mg/kg died as a consequence of gavage trauma. Another female in the 300 mg/kg group died due to causes apparently unrelated to treatment. The mean body weights for both the males and females in the 300 and 600 mg/kg groups were lower than those of the controls by the end the study ($p<0.05$). Mean food consumption was less for the animals in the 600 mg/kg group ($p<0.05$). Clinical observations included irregular respiration and lung noise for the males in the 150 mg/kg group and above and the females in the 300 and 600 mg/kg groups. A dose-related incidence of bronchiolar hypertrophy/hyperplasia was noted as well. These observations were attributed to aspiration of the test material at the time of dosing. The target organ for toxicity was the kidney. In the subchronic toxicity study, oxalate crystal nephrosis, unilateral hydronephrosis and transitional cell hyperplasia were noted in the kidneys of the males in the 300 and 600 mg/kg treatment groups. In the clinical chemistry, the total protein levels were lower for both males and females in the 600 mg/kg group and for the males in the 300 mg/kg group at both time points ($p<0.05$). For the males, the albumin concentration was, likewise, less for both groups at both time points ($p<0.05$). The serum potassium level was reduced for both sexes in the 600 mg/kg group at the end of the study ($p<0.05$). This lower level may have been directly related to the lower urine pH of the animals in the 600 mg/kg group at both time points ($p<0.05$). The males in the high dose group also excreted an increased volume of urine with a decreased osmolality at both time points ($p<0.05$). In conjunction with these effects, the mean absolute kidney weight of the 600 mg/kg males and the relative kidney weights of both the males and female in the 300 and 600 mg/kg groups were greater than that of the controls ($p<0.05$). The immune response of the treated animals was not apparently affected by the treatment. The neurotoxicity study did not reveal any treatment-related neuropathological effects. In the reproduction study, the only parameter in which significance was demonstrated was in the smaller litter size of the 600 mg/kg group ($p<0.05$). However, the mean value was within the historical control range and thus was considered to be of minimal consequence. **Possible adverse effect:** oxalate crystal nephrosis; **Subchronic NOEL:** (M/F) 150 mg/kg/day (based upon the renal effects noted for the males and the lower mean body weights for both sexes in the 300 mg/kg/day treatment group), **Immunotoxicity, Neurotoxicity and Reproduction NOEL:** (M/F) 600 mg/kg/day (no treatment-related effects noted at highest dose tested). Study acceptable. (Moore, 10/13/00)